BRIGHAM AND WOMEN'S HOSPITAL

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R&D100 Judges
c/o Los Alamos National Laboratory
Los Alamos, NM 87545

Dear R&D100 Judges:

I am writing to support the "MESA" technology R&D100 entry. The measurement of protein-drug interactions is key to target-based drug development. These measurements often are difficult to obtain, especially when a mixture of proteins is used. "Label-free" fluorescence or fluorescence measurements obtained without the need for chemically appended fluorescing functional groups, is a significant improvement in the drug identification process.

MESA technology (*Measurement of Enzyme-Substrate Affinities*) is an elegant solution to this unmet need for label-free drug measurement. It works by using x-ray excitation and x-ray fluorescence of heavy atoms. Many drugs contain these heavy atoms that are fluorescent in the x-ray spectrum.

Label-free protein-drug interaction measurements provide a means to answer questions concerning protein target identification during drug discovery and development. Utilizing phenotypic cell-based assays is appealing from a drug discovery point of view. However, one drawback to this approach has been subsequent identification of the molecular target responsible for a particular compound's mechanism of action. Increasingly, regulatory agencies such as the FDA requires that the protein target be identified in order to grant a drug Investigational New Drug (IND) status, i.e. approval for human clinical trials. Traditionally this has involved chemical modification of the ligand with a fluorescent label. However, in many instances installation of the label results in diminished activity of the derivative compared to the parent molecule. MESA can allow label-free measurement of protein-drug interaction useful for target identification. This could unlock tremendous value by simplifying the process of target identification and would encourage increased utilization of cell-based assays in drug discovery.

Label-free measurement of protein-drug interaction has been a longstanding need in the pharmaceutical industry. The preliminary MESA data is promising, and if it can be implemented on an industrial scale, it could significantly affect the development of new lifesaving drugs.

Sincerely,

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